

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
13 January 2005 (13.01.2005)

PCT

(10) International Publication Number
WO 2005/003150 A3

(51) International Patent Classification⁷: **A61K 31/7076**,
31/770

(21) International Application Number:
PCT/US2004/021387

(22) International Filing Date: 2 July 2004 (02.07.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/484,484 2 July 2003 (02.07.2003) US

(71) Applicant (for all designated States except US): **EMORY
UNIVERSITY** [US/US]; 1380 South Oxford Road, N.E.,
Atlanta, GA 30322 (US).

(72) Inventor: and

(75) Inventor/Applicant (for US only): **VINTEN-JO-
HANSEN, Jakob** [US/US]; 1550 Hillside Oak Drive,
Grayson, GA 30017 (US).

(74) Agent: **XIA, Tim, T.**; Morris, Manning & Martin LLP,
1600 Atlanta Financial Center, 3343 Peachtree Road, N.E.,
Atlanta, GA 30326-1044 (US).

(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,
MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG,
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM,
ZW.

(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,
ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI,
FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
GW, ML, MR, NE, SN, TD, TG).

Declaration under Rule 4.17:

as to applicant's entitlement to apply for and be granted a
patent (Rule 4.17(ii)) for the following designations AE,
AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ,
CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE,
EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS,
JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,
MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM,
PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ,
TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM,
ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, NA,
SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE,
BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI patent
(BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG)

Published:

with international search report
before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments

(88) Date of publication of the international search report:
13 October 2005

For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: COMPOSITIONS AND METHODS FOR USE OF A PROTEASE INHIBITOR AND ADENOSINE FOR PREVENT-
ING ORGAN ISCHEMIA AND REPERFUSION INJURY

(57) Abstract: Methods and compositions including combined use of a serine protease inhibitor and adenosine when administered
as a single pharmaceutical composition, concomitantly or sequentially in any order to a living subject for preventing organ ischemia
or reperfusion injury. The methods and compositions disclosed herein can be used in such procedures as cardiac surgery, non-sur-
gical cardiac revascularization, organ transplantation, perfusion, ischemia, reperfusion, ischemia-reperfusion injury, oxidant injury,
cytokine induced injury, shock induced injury, resuscitations injury or apoptosis.

WO 2005/003150 A3

BEST AVAILABLE COPY

From the INTERNATIONAL BUREAU

PCTNOTIFICATION CONCERNING
TRANSMITTAL OF COPY OF INTERNATIONAL
APPLICATION AS PUBLISHED OR REPUBLISHED

To:

XIA, Tim. T.
Morris, Manning & Martin LLP
1600 Atlanta Financial Center
3343 Peachtree Road, N.E.
Atlanta, GA 30326-1044
ETATS-UNIS D'AMERIQUE

BEST AVAILABLE COPY

Date of mailing (day/month/year) 13 October 2005 (13.10.2005)		IMPORTANT NOTICE	
Applicant's or agent's file reference 14507-45204			
International application No. PCT/US2004/021387	International filing date (day/month/year) 02 July 2004 (02.07.2004)	Priority date (day/month/year) 02 July 2003 (02.07.2003)	
Applicant EMORY UNIVERSITY et al			

The International Bureau transmits herewith the following documents:

- ☐ copy of the international application as published by the International Bureau on under No. WO
- ☒ copy of international application as republished by the International Bureau on 13 October 2005 (13.10.2005) under No. WO 2005/003150
For an explanation as to the reason for this republication of the international application, reference is made to INID codes (15), (48) or (88) (as the case may be) on the front page of the attached document.

10/25/05
Rjm

BEST AVAILABLE COPY

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Beate Giffo-Schmitt
Facsimile No. +41 22 740 14 35	Facsimile No. +41 22 338 87 20



From the INTERNATIONAL BUREAU

PCTNOTIFICATION CONCERNING
TRANSMITTAL OF COPY OF INTERNATIONAL
APPLICATION AS PUBLISHED OR REPUBLISHED

To:

XIA, Tim, T.
Morris, Manning & Martin LLP
1600 Atlanta Financial Center
3343 Peachtree Road, N.E.
Atlanta, GA 30326-1044
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year) 13 January 2005 (13.01.2005)		
Applicant's or agent's file reference 14507-45204		IMPORTANT NOTICE
International application No. PCT/US2004/021387	International filing date (day/month/year) 02 July 2004 (02.07.2004)	
Priority date (day/month/year) 02 July 2003 (02.07.2003)		
Applicant EMORY UNIVERSITY et al		

The International Bureau transmits herewith the following documents:

- ☒ copy of the international application as published by the International Bureau on 13 January 2005 (13.01.2005) under No. WO 2005/003150
- ☐ copy of international application as republished by the International Bureau on under No. WO
For an explanation as to the reason for this republication of the international application, reference is made to INID codes (15), (48) or (88) (as the case may be) on the front page of the attached document.

RECEIVED

JAN 21 2005

MORRIS, MANNING & MARTIN

BEST AVAILABLE COPY

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Beate Giffo-Schmitt DOCKETED 1/24/2005 SK
Facsimile No. +41 22 740 14 35	Facsimile No. +41 22 338 87 20

INTERNATIONAL SEARCH REPORT

Inter

PCT/US04/21387

A. CLASSIFICATION OF SUBJECT MATTER IPC(7) : A61K 31/7076, 31/70 US CL : 514/46, 45, 43; 536/27.6 According to International Patent Classification (IPC) or to both national classification and IPC														
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) U.S. : 514/46, 45, 43; 536/27.6 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) STN Electronic Database														
C. DOCUMENTS CONSIDERED TO BE RELEVANT														
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.												
X	STN ABSTRACT: ACCESSION NUMBER: 87293025 MEDLINE, DOCUMENT NUMBER: PubMed ID: 3303451 TITLE: Assessment of potential therapies for acute T-2 toxicosis in the rat. AUTHOR: Poppenga et al.; Toxicon : official journal of the International Society on Toxinology, (1987) 25 (5) 537-46 (see abstract).	4, 5												
X	STN ABSTRACT: ACCESSION NO.: 1989:471310 CAPLUS, DOCUMENT NUMBER: 111:71310, TITLE: The effects of apertinin on follicle-stimulating hormone binding and signal transduction in bovine calf testis. AUTHOR: Grasso et al., Endocrinology (1989), 125 (1), 117-25.	21, 22												
Y	STN ABSTRACT: ACCESSION NO: 2002 303480 CAPLUS DOCUMENT NO: 138:66369 TITLE: LEX032, A Novel Recombinant Scorpion, Protects the Brain after Transient Focal Ischemia, AUTHOR(S): Weaver et al., Microvascular Research (2002), 63 (3), 237-334, see abstract.	1-3, 7-17												
A		18-34												
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.														
<table border="1"><thead><tr><th>Special categories of cited documents</th><th></th></tr></thead><tbody><tr><td>"A" document defining the general state of the art which is not considered to be of particular relevance</td><td>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</td></tr><tr><td>"E" earlier application or patent published on or after the international filing date</td><td>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone</td></tr><tr><td>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</td><td>"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art</td></tr><tr><td>"O" document referring to an oral disclosure, use, exhibition or other means</td><td>"Z" document member of the same patent family</td></tr><tr><td>"P" document published prior to the international filing date but later than the priority date claimed</td><td></td></tr></tbody></table>			Special categories of cited documents		"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention	"E" earlier application or patent published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone	"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art	"O" document referring to an oral disclosure, use, exhibition or other means	"Z" document member of the same patent family	"P" document published prior to the international filing date but later than the priority date claimed	
Special categories of cited documents														
"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention													
"E" earlier application or patent published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone													
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art													
"O" document referring to an oral disclosure, use, exhibition or other means	"Z" document member of the same patent family													
"P" document published prior to the international filing date but later than the priority date claimed														
Date of the actual completion of the international search 05 August 2005 (05.08.2005)		Date of mailing of the international search report 24 AUG 2005												
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230		Authorized officer Michael C. Henry Telephone No. 703 308-1235												

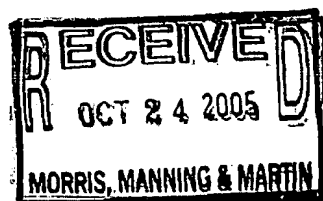
BEST AVAILABLE COPY

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US04/21387

C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	STN ABSTRACT: ACCESSION NO: 2000178187 MEDLINE	1-3, 7-17
—	DOCUMENT NUMBER: PubMed ID: 10710542	
A	TITLE: Protective effects of renal ischemic preconditioning and adenosine pretreatment: role of A(1) and A(3) receptors. AUTHOR: Lee et al., American Journal of Physiology. Renal Physiology, (2000 March) 278 (3) F380-7, see abstract.	6, 18-34



BEST AVAILABLE COPY